

## **AMENDMENTS TO THE CLAIMS:**

The following listing of claims will replace all prior versions and listings of claims in this application.

1. (Withdrawn) A method for diagnosing a nervous system disorder in a subject comprising:
  - a. contacting a sample from said subject with an aPKC specific probe,
  - b. detecting the binding of said probe to said sample to determine the activity of said aPKC in said sample,
  - c. contacting a control sample with said aPKC specific probe,
  - d. detecting the binding of said probe to said control sample to determine the activity of said aPKC in said control sample, and
  - e. comparing the activity of said aPKC in Step b with the activity of said aPKC in Step d, wherein if the activity of said aPKC in Step b is different from the activity of said aPKC in Step d, a nervous system disorder in said subject is present.
2. (Withdrawn) The method of Claim 1, wherein Step d is preformed by quantifying a label attached to said probe.
3. (Withdrawn) The method of Claim 1, wherein said disorder is a neurodegenerative, neurological or psychiatric disorder.
4. (Withdrawn) The method of Claim 1, wherein said probe is an antibody or a nucleic acid sequence.

5. (Withdrawn) The method of Claim 1, wherein said sample is a human tissue or tissue extract or body fluid.

6. (Withdrawn) The method of Claim 5, wherein said tissue is postmortem autopsy tissue or brain biopsy tissue.

7. (Withdrawn) The method of Claim 1, wherein said nervous system disorder is selected from the group consisting of Alzheimers disease (AD), Pick's disease (PiD), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), Parkinson's disease (PD) and multisystem atrophy (MSA).

8. (Withdrawn) A method for identifying a compound useful for modulating the activity of an aPKC comprising:

- a. providing cells wherein said aPKC gene is expressed,
- b. incubating said cells with a candidate compound for a sufficient time to induce a change in the activity of a aPKC in said cells,
- c. incubating said cells as in Step b, in the absence of said candidate compound or in the presence of a control compound,
- d. contacting said cells from Step b and Step c with an equal amount of an aPKC-specific probe,
- e. detecting the binding of said probe to said cells to determine the activity of said aPKC in said cell from Step b and Step c, and
- f. comparing the activity of said aPKC in said cells, wherein if the activity of said aPKC in said cells from Step b is different from the activity of said aPKC in said cells from Step c, said candidate compound modulates aPKC.

9. (Withdrawn) The method of Claim 8, wherein said compound is a peptide, a small molecule or a macromolecule.

10-11. (Canceled)

12. (Withdrawn) A method for treating a nervous system disorder in a subject comprising:

- a. inserting an aPKC sequence into an expression vector, and
- b. administering said vector from Step a to said subject.

13. (Canceled)

14. (Withdrawn) The method of Claim 12, wherein said expression vector is administered via intraventricular, intravenous, inhalation, dermal or oral route.

15. (Withdrawn) The method of Claim 12, where the dosage to be administered is sufficient to maintain said aPKC activity at a normal level.

16. (Withdrawn) The method of Claim 15, wherein said normal level is an amount of said aPKC from about 0.005% to about 0.05% of total protein in a sample from said subject.

17. (Canceled)

18. (Withdrawn) The method Claim 1 or 12, wherein said disorder is characterized by abnormal aPKC activity.

19. (Withdrawn) The method of Claim 18, wherein said abnormal aPKC activity comprises phosphorylation of protein tau and co-localization with neurofibrillary tangles (NFT).

20. (Withdrawn) The method of Claim 1 or 12, wherein said disorder is selected from the group consisting of Alzheimer's disease (AD), Pick's disease (PiD), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), Parkinson's disease (PD) and multisystem atrophy (MSA).

21. (Withdrawn) The method of Claim 1 or 12, wherein said aPKC is PKM $\zeta$ .

22. (Currently amended) ~~An~~A purified antibody which binds to an atypical isoform of an a protein kinase C (aPKC) molecule, wherein the aPKC is protein kinase M zeta (PKM $\zeta$ ) or a functional derivative thereof.

23. (Canceled)

24. (Withdrawn) A method for treating a nervous system disorder of a subject comprising:

- a. generating an antibody against PKM $\zeta$ , and
- b. administering said antibody or a functional fragment thereof to said subject.

25. (Withdrawn) A method for constructing an animal model of neurological dysfunction comprising:

- a. constructing a transgenic animal having an altered aPKC amount, localization or activity,
- b. treating said transgenic animal from Step a with a candidate compound

- c. treating said transgenic animal from Step a with a control compound,
- d. assaying said transgenic animals from Steps b and c for a biochemical or behavioral changes, and
- e. comparing the results from Step d, wherein differences are indicative the efficacy of said candidate compound in treatment of said neurological dysfunction.

26. (Withdrawn) The method of Claim 25, wherein said transgenic animal is a knock-out mouse lacking aPKC.

27. (Withdrawn) The method of Claim 25, wherein said transgenic animal is a mouse that overexpresses an aPKC.

28. (Withdrawn) The method of any one of Claims 25-27, wherein said aPKC is a wild type or mutant aPKC.

29. (Withdrawn) The method of Claim 25, wherein said biochemical change is tau phosphorylation.

30. (Withdrawn) The method of Claim 25, wherein said behavioral change is a memory deficit.

31. (Withdrawn) A method for screening DNA for a mutation or polymorphisms in the DNA sequence of the aPKC genes and regions regulating the expression of these genes comprising:

- a. isolating DNA from a sample of a subject,
- b. sequencing said DNA, and

- c. comparing said sequence to a reference DNA sequence, whereby a difference between the DNA sequence derived from said subject and the reference sequence is indicative of genetic susceptibility to a neurological or psychiatric disorder.

32. (Withdrawn) The method of Claim 31, wherein Step c is performed by comparing single nucleotide polymorphisms (SNPs) on said sequence to SNPs on said reference DNA sequence.

33. (Withdrawn) The method of Claim 31, wherein said reference DNA sequence is a human genomic sequence of PKC iota/lambada set forth in SEQ ID NO:6.

34. (Withdrawn) The method of Claim 31, wherein said reference DNA sequence is a human genomic sequence of PKC zeta set forth in SEQ ID NO:7.

35. (Withdrawn) A method for diagnosing cancer comprising:

- a. contacting a tumor sample from a subject with an aPKC specific probe,
- b. detecting the binding of said probe to said tumor sample to quantify the activity of said aPKC in said tumor sample,
- c. contacting a control sample with said aPKC specific probe,
- d. detecting the binding of said probe to said control sample to quantify the activity of said aPKC in said control sample, and
- e. comparing said activity of said aPKC in Step b with said activity of said aPKC in Step d, wherein the difference of the activity of said aPKC is indicative of the type or the staging of said cancer.

36. (Withdrawn) The method of Claim 35. wherein said cancer is selected from the group consisting of neuroblastoma, oligodendroglioma, meningioma, lymphoma (myeloma), leukemia, melanoma, squamous cell carcinoma, hepatocellular carcinoma, parathyroid tumors, pheochromocytoma, paraganglioma, intravascular lymphomatosis, breast cancer, liver cancer, lung cancer, prostate cancer, bladder cancer, ovarian cancer, endometrial cancer, head and neck cancer, colorectal cancer and pancreatic cancer.

37. (Withdrawn) The method of Claim 35 or 36, wherein said method comprises gene therapy